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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/724,396	11/28/2000	James F. Young	10271-007-999	8214

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JONES DAY
222 EAST 41ST ST
NEW YORK, NY 10017

EXAMINER
CHEN, STACY BROWN

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 04/05/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/724,396	YOUNG ET AL.	
	Examiner	Art Unit	
	Stacy B Chen	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 January 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *73,74,85-94,99-110,180,181,186,189-191 and 231-263* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *73,74,85-94,99-110,180,181,186,189-191 and 231-263* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *28 November 2000* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *1/20/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment filed January 20, 2004 is acknowledged and entered. Claims 73, 74, 85-94, 99-110, 180-181, 186, 189-191, 231-263 are pending and examined.

2. The objection to claims 89, 91 and 187 is withdrawn in view of Applicant's amendment. The rejection of claim 187 under 35 U.S.C. 112, second paragraph, is moot in view of the cancellation of claim 187. The rejection of claims 73, 85, 86, 89, 90, 91, 92, 99, 100 and 103-106 under 35 U.S.C. 103(a) as being unpatentable over MedImmune, Inc. Synagis™ package insert in view of Lam *et al.* (*Proc. Int'l. Symp. Rel. Bioact. Mater.*, 1997, 24:759-790) is withdrawn in view of Applicant's amendment. The rejection of claims 74, 87, 88, 93, 94, 101, 102, 107-110, 180-181, 186, 187, 189, 190 and 191 under 35 U.S.C. 103(a) as being unpatentable over the Package Insert in view of Lam, and further in view of Gonzalez *et al.* (6,117,980) is withdrawn in view of Applicant's amendment. In view of Applicant's amendments, the following new grounds of rejection are made.

Claim Rejections - 35 USC § 103

3. Claims 73, 74, 85-94, 99-110, 180-181, 186 and 189-191 are rejected under 35 U.S.C. 103(a) as being unpatentable over Johnson (5,824,307) and MedImmune, Inc. Synagis™ Package Insert (of record) in view of Tracy *et al.* (6,565,888). The claims are drawn to a sustained release formulation comprising palivizumab and can be adapted for pulmonary delivery with a suitable carrier. Also claimed are methods of preventing RSV infection, and treating or ameliorating one or more symptoms associated with RSV infection in human subjects by administering to the lungs the sustained release composition. Administration can be

intramuscularly, intravenously or by nebulizer/inhaler. Also claimed is a method of administering the sustained release composition in a concentration resulting in at least 20 ng per mg of lung protein at least 20 days after the administration of the first dose and prior to the administration of a second dose.

Johnson teaches prevention and/or treatment of RSV infection via administration of palivizumab intramuscularly, intravenously, intranasally and inhaled (abstract and col. 4, lines 28-41). Johnson teaches that the neutralizing humanized monoclonal antibody can be administered to humans with a pharmaceutical carrier (see claims 1-30). The Package Insert, of record, teaches that palivizumab is administered to infants at high risk of RSV-related hospitalization, bronchopulmonary dysplasia, premature birth or congenital heart disease (see Clinical Studies). Johnson and the Package Insert are silent on the formulation of the antibody into a sustained release composition and the resulting concentration of the antibody after administration.

Tracy teaches the administration of targeted delivery of labile agents in sustained release compositions (abstract). Biologically active agents include viral antigens (col. 18, claim 41) and antibodies (col. 7, lines 34-52). These sustained release compositions can be administered by any route including oral, parenteral, inhalation or injection (col. 4, lines 16-26).

It would have been obvious to incorporate the sustained release composition formulation into the method/composition of Johnson and the palivizumab Package Insert. One would have been motivated by Tracy's teaching that the sustained release compositions can be antibodies and vaccines, for example (col. 7, lines 41 and 49). Although Tracy does not specifically disclose viral antibodies, one of ordinary skill in the art would have known at the time of

invention that viral antibodies were within the scope of labile agents listed in column 7. Further, one of ordinary skill would have recognized that palivizumab is a passive vaccine, thereby inclusive under the term "vaccine" in column 7, line 49. One would have had a reasonable expectation of success that the antibodies would work in the sustained release composition of Tracy, because Tracy uses antibodies. Regarding the resulting concentration of the antibody after administration, it is well within the capabilities of one of ordinary skill to optimize the dosages to result in desired concentrations in the body.

4. Claims 231-263 are rejected under 35 U.S.C. 103(a) as being unpatentable over Johnson (5,824,307) and MedImmune, Inc. Synagis™ Package Insert (of record) in view of Tracy *et al.* (6,565,888) as applied to claims 73, 74, 85-94, 99-110, 180-181, 186 and 189-191 above, and further in view of Lam *et al.* (*Proc. Int'l. Symp. Rel. Bioact. Mater.*, 1997, 24:759-790). The claims are drawn to methods of preventing RSV infection, treating or ameliorating symptoms of RSV infection in humans by administering a sustained release formulation comprising a fragment of palivizumab, specifically, a Fab fragment which by nature includes the variable domains of the heavy and light chains. The cited references of Johnson, the Package Insert and Tracy are silent on the administration of a F(ab') fragment.

However, Lam teaches the administration of anti-VEGF Fab fragments. It would have been obvious to use the Fab fragment from palivizumab. One would have been motivated to use the Fab fragment because all of the variable portions are present which result in the neutralization of RSV (Johnson, abstract). One would have had a reasonable expectation of success that a Fab fragment would work because it is well known in the art that the Fab

fragment(s) can be substituted for the full-length antibody, as evidenced by Lam, who administers fragments successfully.

Applicant's arguments have been carefully considered. Applicant's substantive arguments are primarily directed to the assertion that:

- The anti-VEGF Fab fragment of Lam may have a different structure than the fragment of palivizumab.
    - In response, a Fab fragment is expected to have the variable regions of the light and heavy chains. Lacking evidence to the contrary, one would reasonably expect that the Fab fragment from an anti-VEGF antibody and palivizumab would have similar structures.
- The function of the anti-VEGF Fab fragment and the function of the palivizumab Fab fragment are different. Lam's fragment binds a cytokine normally found in the body. Palivizumab (Fab) binds an antigen not normally found in the body. Applicants submit that one would expect differences in structure and function to result in different methods of administration/dosing to achieve the desired prophylactic/therapeutic effect.
    - In response, palivizumab is administered to a patient because it is expected that the patient will encounter RSV and that an RSV antigen will be bound and neutralized by the palivizumab Fab fragment. Even though RSV is not present in the body as frequently as Lam's cytokine, Applicant's method of administering/dosing a Fab fragment is not patentably distinguishable. The claims are directed to a method of administering a Fab fragment having no

particulars in the method steps that distinguish it from the administration of an anti-VEGF Fab fragment.

Conclusion

5. No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Papers relating to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 located in Crystal Mall 1. The Fax number for Art Unit 1648 is (703) 872-9306. All Group 1600 Fax machines will be available to receive transmissions 24 hrs/day, 7 days/wk. Please note that the faxing of such papers must conform with the Notice published in the Official Gazette, 1096 OG 30, (November 15, 1989).

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Stacy B. Chen, whose telephone number is (571) 272-0896. The Examiner can normally be reached on Monday through Friday from 7:30 AM-4:00 PM, (EST). If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's Supervisor, James C. Housel, can be reached at (571) 272-0902. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

James C. Housel 4/2/04

SBC

Stacy B. Chen
March 26, 2004

JAMES HOUSEL
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600